# Updates to the pediatric recommendation for use of pneumococcal vaccines

ACIP Pneumococcal Vaccines Workgroup

June 25, 2008

# Outline

- Review the list of underlying medical conditions for which PPV23 is recommended after PCV7
- Current rates and serotypes of invasive pneumococcal disease (IPD) in children
- Clarify the recommendation language for use of PPV23 after PCV7 in Alaska Native and American Indian (AN/AI) children
- Clarify the recommended time interval for PPV23 revaccination in high risk children
- Discuss use of PCV7 in HIV-infected, school-aged children

**TABLE 8. Summary of recommendations for use of 7-valent pneumococcal conjugate vaccine (PCV7) among infants and children**

**Children for whom PCV7 is recommended**

All children aged ≤23 mos

Children aged 24–59 mos with the following conditions:

- Sickle cell disease and other sickle cell hemoglobinopathies, congenital or acquired asplenia, or splenic dysfunction
- Infection with human immunodeficiency virus
- Immunocompromising conditions, including
  - Congenital immunodeficiencies: B- (humoral) or T-lymphocyte deficiency; complement deficiencies, particularly c1, c2, c3, and c4 deficiency; and phagocytic disorders, excluding chronic granulomatous disease
  - Renal failure and nephrotic syndrome
  - Diseases associated with immunosuppressive therapy or radiation therapy, including malignant neoplasms, leukemias, lymphomas, and Hodgkin's disease; or solid organ transplantation
- Chronic illness, including
  - Chronic cardiac disease, particularly cyanotic congenital heart disease and cardiac failure
  - Chronic pulmonary disease, excluding asthma unless on high dose corticosteroid therapy
  - Cerebrospinal fluid leaks
  - Diabetes mellitus

- Cochlear implant recipients

**Children for whom PCV7 should be considered**

All children aged 24–59 mos, with priority given to

- Children aged 24–35 mos
- Children of Alaska Native or American Indian descent
- Children of African-American descent
- Children who attend group day care centers*

* Defined as a setting outside the home where a child regularly spends ≥4 hours per week with ≥2 unrelated children under adult supervision.

*** ACIP.MMWR 2000;49(RR-9)**

# MMWR 2000;49(RR-9) Table 8 - list of high risk conditions

- In October 2007, the ACIP recommended that all children aged <5 years should receive PCV7*
- Therefore, the list of medical high risk conditions in Table 8 was simplified to a list of children who are recommended to receive PPV23 after their PCV7 series at age ≥2 years

*MMWR 2008:57;343-4

**TABLE 12. Schedule for vaccination using 23-valent polysaccharide vaccine (PPV23) for children aged ≥2 years who have previously received the 7-valent conjugate vaccine (PCV7)**

| Population | Schedule for PPV23 | Revaccination with PPV23* |
|---|---|---|
| Healthy children | None† | No |
| Children with sickle cell disease or anatomic or functional asplenia; immunocompromised;§ or who are infected with human immunodeficiency virus | 1 dose of PPV23 administered at age ≥2 yrs and ≥2 mos after last dose of PCV7 | Yes¶ |
| Persons with chronic illness§ | 1 dose of PPV23 administered at age ≥2 yrs and ≥2 mos after last dose of PCV7 | Not recommended |

* Recommendations for revaccination are adapted from CDC. Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1997;46(No. RR-8):12.

† Health-care providers of Alaska Natives and American Indians should consider whether these children would benefit by the additional coverage provided by the expanded serotypes in PPV23 (see recommendations regarding Alaska Natives and American Indians).

§ See Table 8.

¶ Regardless of when administered, a second dose of PPV23 should not be administered <3 years after the previous PPV23 dose. If the patient is aged >10 years, one revaccination should be administered ≥5 years after the previous PPV23 dose. If the patient is aged ≤10 years, one revaccination 3–5 years after previous dose should be considered (**Sources:** CDC. Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 1997;46[No. RR-8]:1–24; and American Academy of Pediatrics.



*** ACIP.MMWR 2000;49(RR-9)**

# Current ACIP recommendation for use of PPV23 in children who have received PCV7

- *"Children who have completed PCV7 vaccination series before age 2 years and who are among risk groups for which PPV23 is already recommended should receive one dose of PPV23 at age 2 years"*
- *"These groups at high risk include children with SCD, children with functional or anatomic asplenia, children who are HIV-infected, and children who have immunocompromising or chronic diseases"*
- *"For children of Alaska Native or American Indian descent, addition of PPV23 after PCV7 can be considered"*



**MMWR 2000 / 49(RR-09);1-38**

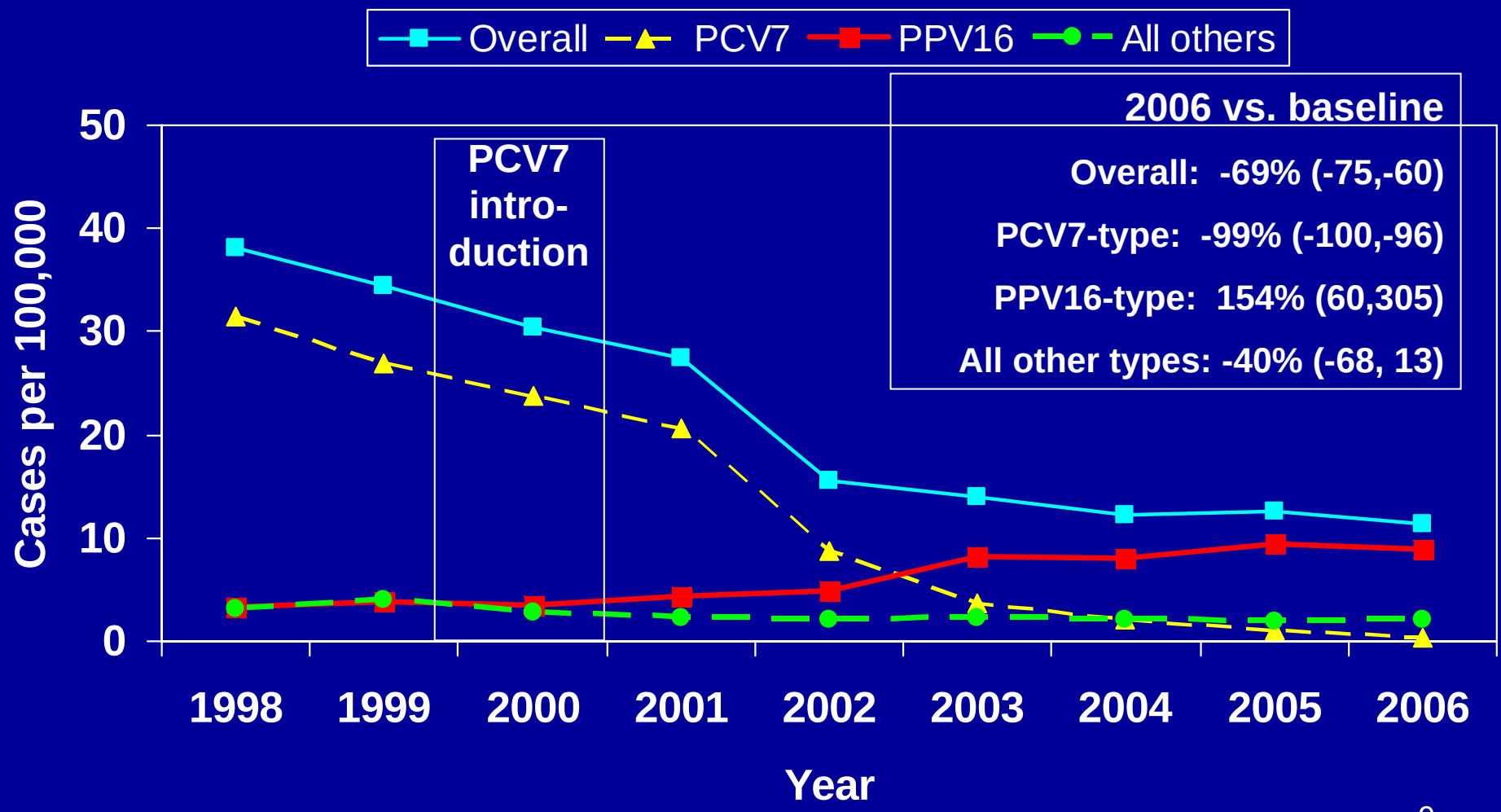
# Current ACIP recommendation for use of PPV23 in children who have received PCV7

- *"Although data regarding safety of PPV23 administered after PCV7 are limited, the opportunity to provide additional serotype coverage among these children at very high risk justifies use of the vaccines sequentially."*

**MMWR 2000 / 49(RR-09);1-38**

# Current rates and serotypes causing IPD in children aged ≥2 years

# Rates of invasive pneumococcal disease among children aged 24-59 months, by serotype,1998/99-2006






Data source: CDC, Active Bacterial Core surveillance, unpublished, 2008

# Proportion of IPD cases among children 24-59 months-old who had underlying medical conditions* 1998-2006

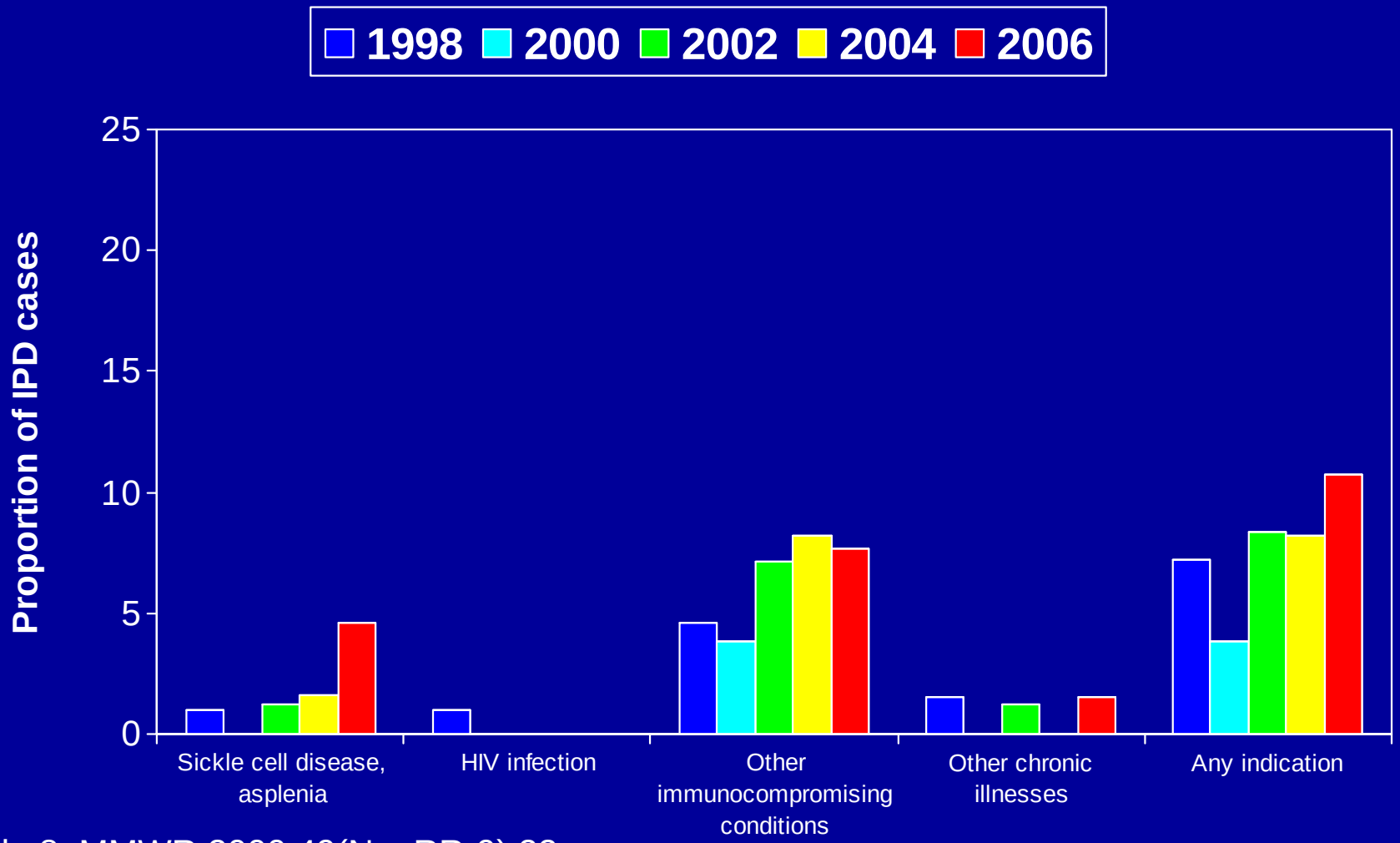



*Table 8, MMWR 2000;49(No. RR-9):22



Data source: CDC, Active Bacterial Core surveillance, unpublished, 2008

# Proportion of IPD cases caused by indicated serotypes among children 24-59 months-old with high risk medical conditions* (N=7), 2006

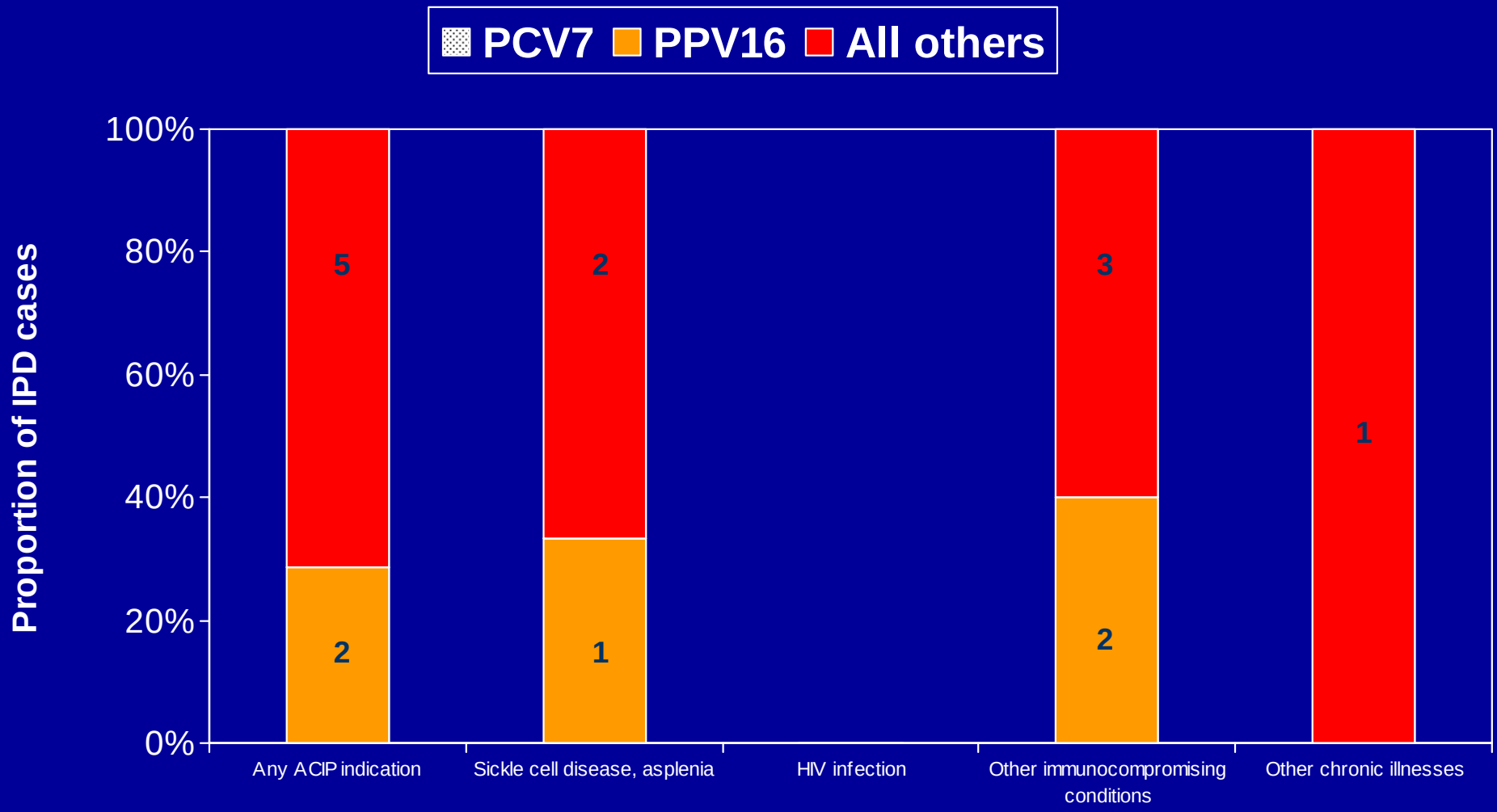



*Table 8, MMWR 2000;49(No. RR-9):22

Data source: CDC, Active Bacterial Core surveillance, unpublished, 2008

**TABLE 8. Summary of recommendations for use of 7-valent pneumococcal conjugate vaccine (PCV7) among infants and children**

| **Children for whom PCV7 is recommended** |
|---|
| All children aged ≤23 mos |
| Children aged 24–59 mos with the following conditions: |
| • Sickle cell disease and other sickle cell hemoglobinopathies, congenital or acquired asplenia, or splenic dysfunction |
| • Infection with human immunodeficiency virus |
| • Immunocompromising conditions, including |
| — Congenital immunodeficiencies: B- (humoral) or T-lymphocyte deficiency; complement deficiencies, particularly c1, c2, c3, and c4 deficiency; and phagocytic disorders, excluding chronic granulomatous disease |
| — Renal failure and nephrotic syndrome |
| — Diseases associated with immunosuppressive therapy or radiation therapy, including malignant neoplasms, leukemias, lymphomas, and Hodgkin's disease; or solid organ transplantation |
| • Chronic illness, including |
| — Chronic cardiac disease, particularly cyanotic congenital heart disease and cardiac failure |
| — Chronic pulmonary disease, excluding asthma unless on high dose corticosteroid therapy |
| — Cerebrospinal fluid leaks |
| — Diabetes mellitus |
| **Children for whom PCV7 should be considered** |
| All children aged 24–59 mos, with priority given to |
| • Children aged 24–35 mos |
| • Children of Alaska Native or American Indian descent |
| • Children of African-American descent |
| • Children who attend group day care centers* |

* Defined as a setting outside the home where a child regularly spends ≥4 hours per week with ≥2 unrelated children under adult supervision.

*** ACIP.MMWR 2000;49(RR-9)**

# Considerations regarding use of PPV23 in children with asthma

- Diagnosis of pediatric asthma is difficult
  - Varying definitions, no standard
  - Many children outgrow wheezing
- About 6.8 million children are reported to have asthma[1]
- Available data from one study conducted during 1995-2002 suggests moderately increased risk [2]
  - Age 2-4 years: odds ratio 2.3 (1.4-4.0)
  - Age 5-17 years: odds ratio 4.0 (1.5-10.7)
- Current rates of IPD very low in children aged ≥2 years because of direct and indirect effects of routine PCV7
- Lack of data on effectiveness of PPV23 following PCV7 in children

1) National Health Interview Survey, 2006
2) Talbot et al, N Engl J Med 2005

# Proposed recommendation - children with asthma

- The work group recommends that children aged 2-18 years who have “asthma without high dose corticosteroid therapy” should not be administered PPV23 after their PCV7 series
- No changes are proposed to the list of children with underlying medical conditions who are recommended to receive PPV23 after their PCV7 series

**TABLE 12. Schedule for vaccination using 23-valent polysaccharide vaccine (PPV23) for children aged ≥2 years who have previously received the 7-valent conjugate vaccine (PCV7)**

| Population | Schedule for PPV23 | Revaccination with PPV23* |
|---|---|---|
| Healthy children | None† | No |
| Children with sickle cell disease or anatomic or functional asplenia; immunocompromised;§ or who are infected with human immunodeficiency virus | 1 dose of PPV23 administered at age ≥2 yrs and ≥2 mos after last dose of PCV7 | Yes¶ |
| Persons with chronic illness§ | 1 dose of PPV23 administered at age ≥2 yrs and ≥2 mos after last dose of PCV7 | Not recommended |

* Recommendations for revaccination are adapted from CDC. Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1997;46(No. RR-8):12.

† Health-care providers of Alaska Natives and American Indians should consider whether these children would benefit by the additional coverage provided by the expanded serotypes in PPV23 (see recommendations regarding Alaska Natives and American Indians).

§ See Table 8.

¶ Regardless of when administered, a second dose of PPV23 should not be administered <3 years after the previous PPV23 dose. If the patient is aged >10 years, one revaccination should be administered ≥5 years after the previous PPV23 dose. If the patient is aged ≤10 years, one revaccination 3–5 years after previous dose should be considered (**Sources:** CDC. Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 1997;46[No. RR-8]:1–24; and American Academy of Pediatrics.

# Current recommendation for use of PPV23 after PCV7 in Alaska Native/American Indian children

- *"For children of Alaska Native or American Indian descent, addition of PPV23 after PCV7 can be considered"*
- *"Health care providers of Alaska Natives and American Indians should consider whether these children would benefit by the additional coverage provided by the expanded serotypes in PPV23."*

**MMWR 2000 / 49(RR-09);1-38**

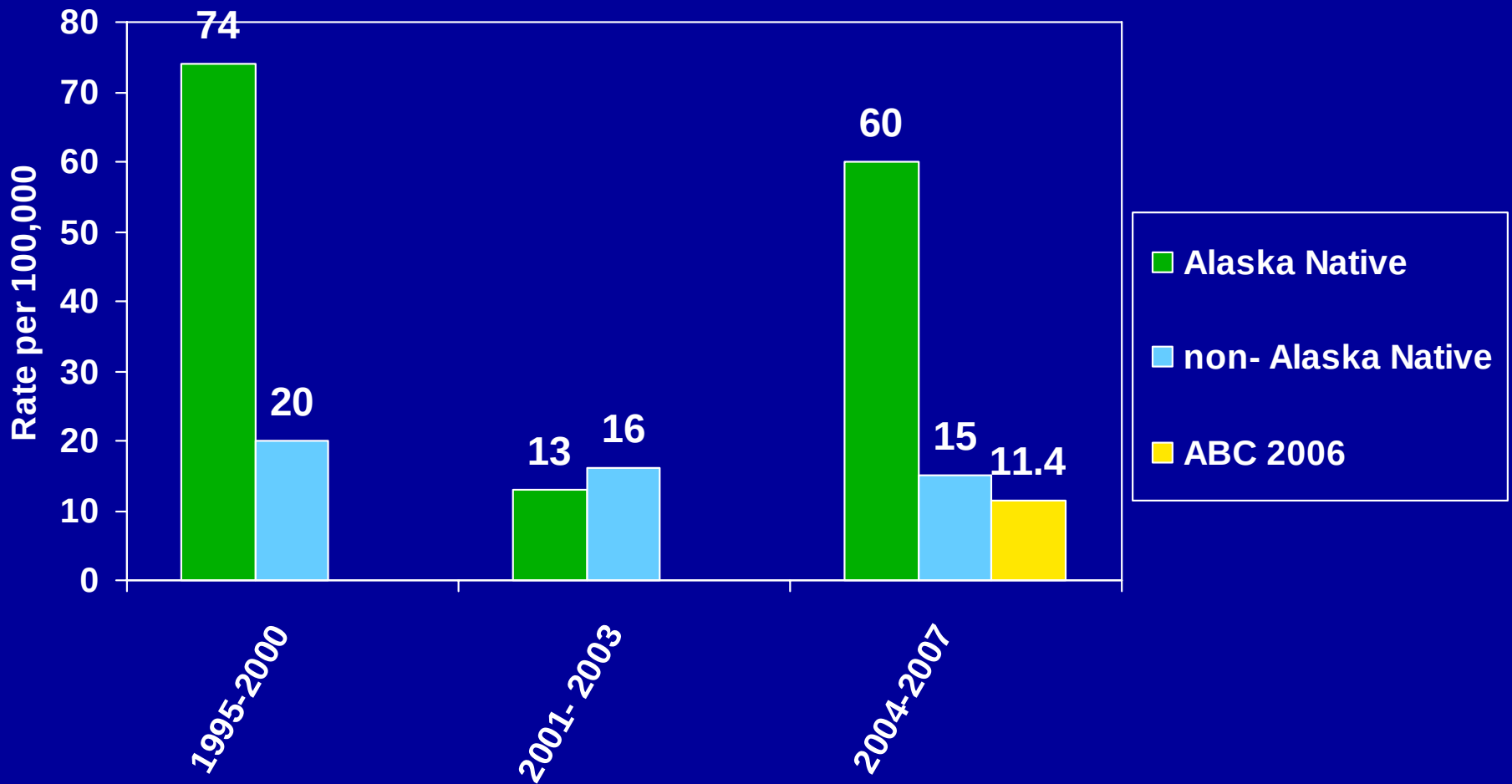
# Considerations for revising the PPV23 recommendation for AN/AI children

- Data on increased risk of pneumococcal disease are limited to Alaska Native, White Mountain Apache and Navajo populations
- Current ACIP language lacks specificity
  - All Alaska Native and American Indian groups are not at equal risk
  - Unclear how “American Indian descent” is defined
  - Burden of decision seems to rest on individual practitioner

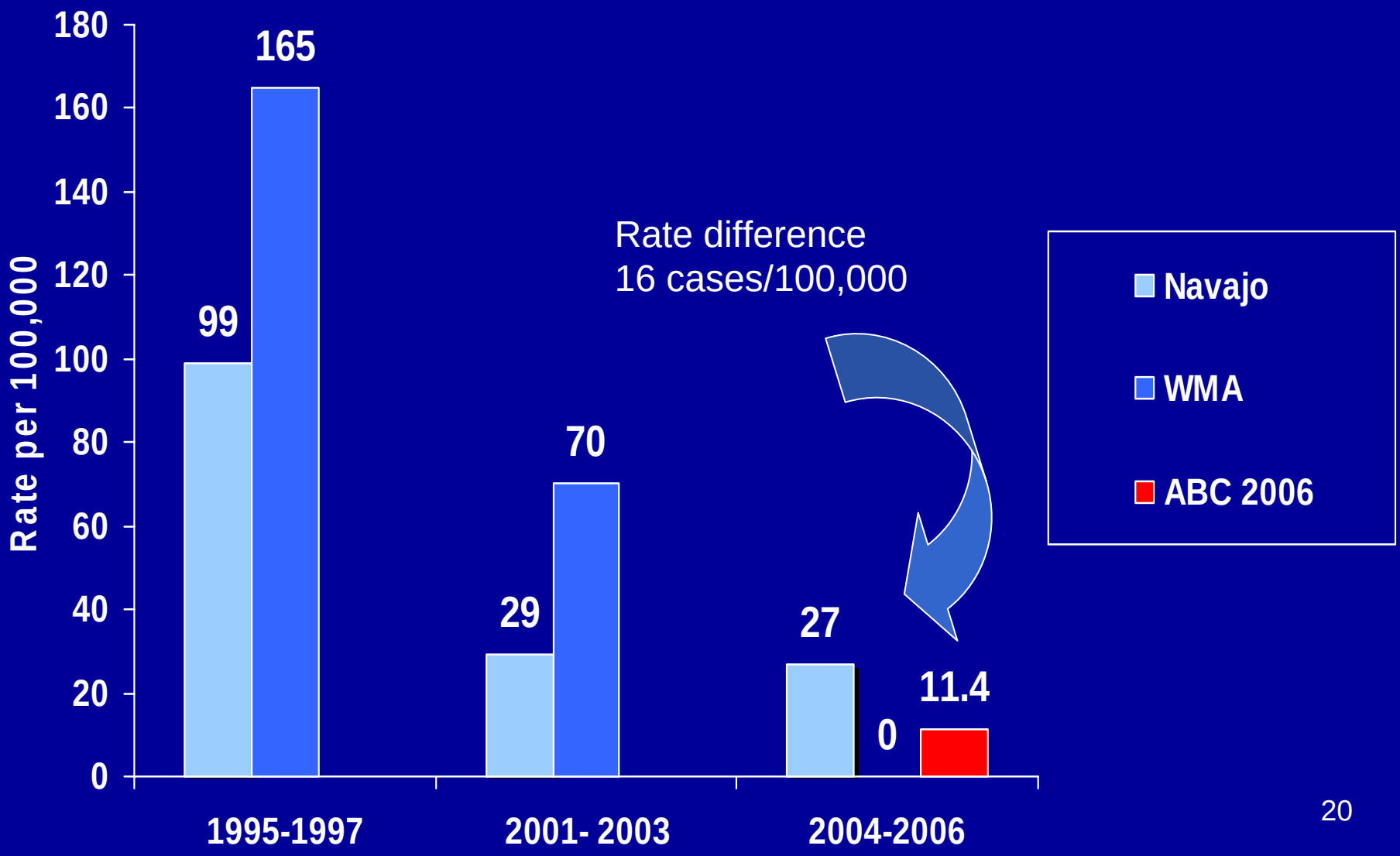
# Current practice

- Current clinical practice among children ≥2 years in Alaska Native, White Mountain Apache and Navajo populations
- Despite the recommendation to consider PPV23, it is NOT routinely given to all AN/AI children in these populations, except for those with high risk medical conditions

# IPD Rates, 2 - 4 yrs, Alaska Natives vs. non-Natives and the general U.S. population



# IPD Rates among children aged 2-4 years, Navajo, WMA and the general U.S. population



# Summary, IPD among AN/AI children aged 2-4 years

- Rates of non-PCV7 disease increasing in AN but unchanged in Navajo and WMA
  - Small numbers of cases
- Overall rates 24-60 per 100,000 per year
  - 2-5 fold compared with the general U.S. population
- 80-90% of IPD due to PPV23 serotypes

# Summary of Workgroup's considerations – AI/AN children

- Alaska Native children
  - PPV23 is a potentially useful tool for preventing IPD in 2-4 year old Alaska Native children
  - Recent increases in non-PCV7 type disease have increased interest in PPV23
- Navajo and WMA children
  - Rates of PPV23 type disease, although higher (for some time-periods) than general US reflect a small number of cases
  - PPV23 was not routinely implemented in these populations before PCV7 when rates were significantly higher
- Concerns
  - PPV23 effectiveness after PCV7 is unknown
  - Potential immunological hyporesponsiveness after PPV23

**TABLE 12. Schedule for vaccination using 23-valent polysaccharide vaccine (PPV23) for children aged ≥2 years who have previously received the 7-valent conjugate vaccine (PCV7)**

| Population | Schedule for PPV23 | Revaccination with PPV23* |
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| Healthy children | None† | No |
| Children with sickle cell disease or anatomic or functional asplenia; immunocompromised;§ or who are infected with human immunodeficiency virus | 1 dose of PPV23 administered at age ≥2 yrs and ≥2 mos after last dose of PCV7 | Yes¶ |
| Persons with chronic illness§ | 1 dose of PPV23 administered at age ≥2 yrs and ≥2 mos after last dose of PCV7 | Not recommended |

* Recommendations for revaccination are adapted from CDC. Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1997;46(No. RR-8):12.

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# Revaccination with PPV23 in children – current recommendation

- *"Immunocompromised children or children with SCD or functional or anatomic asplenia should be revaccinated with PPV23"*
- *"If the child is aged ≤10 years, one revaccination should be considered 3-5 years after the previous dose of PPV23"*
- *"Data are limited regarding adverse events related to second dose of PPV23 administered after PCV7. Health care providers should not administer a second dose of PPV23 any earlier than 3 years after the initial dose of PPV23".*

**MMWR 2000 / 49(RR-09);1-38**

# Summary of considerations – PPV23 revaccination in children

- The “3-5 year interval” may be confusing
- Recommendation to revaccinate high risk children 3 years after the first dose was based on immunologic data from the 1980s indicating rapid antibody decline after PPV vaccination in children at highest risk
- 5 of 6 studies conducted in the 1970s and 1980s observed lower antibody concentrations for some serotypes with a second PPV dose*
- Clinical effectiveness of PPV23 revaccination is unknown

*Reviewed in: O’Brien et al. Lancet Infect Dis 2007;7:597-606

# Children aged ≥5 years - current ACIP recommendation

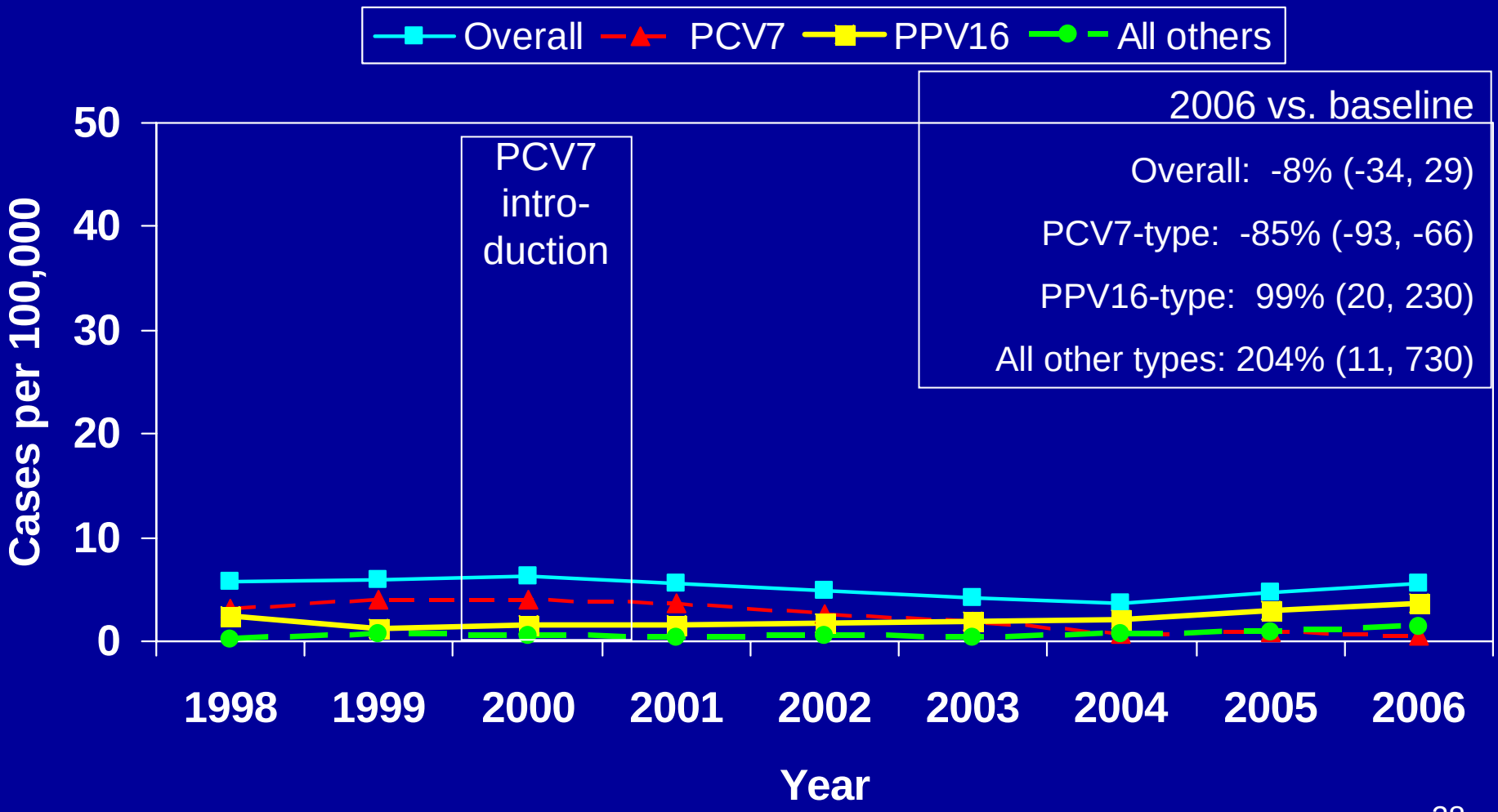
- Data are limited regarding efficacy of PCV7 in children aged ≥ 5 years
  - PCV5 immunogenic in children 2-9 years
  - PCV7 immunogenic in children aged 2-13 years with recurrent respiratory infections
- PCV7 is currently licensed for use up to age 9 years
- "Administering PCV7 to older children with high-risk conditions is not contraindicated"
- "Current data do not support replacing PPV23 with PCV7 among older children and adults"

**MMWR 2000 / 49(RR-09);1-38**

# AAP Report of the Committee on Infectious Diseases, “Redbook”, 2006

- PCV7 safe and immunogenic up to 13 yrs old
  - Administration of a single dose of PCV7 to children of any age, particularly children who are at high risk of IPD, is not contraindicated
    - …immunization with a single dose of PCV7 or PPV23 is acceptable

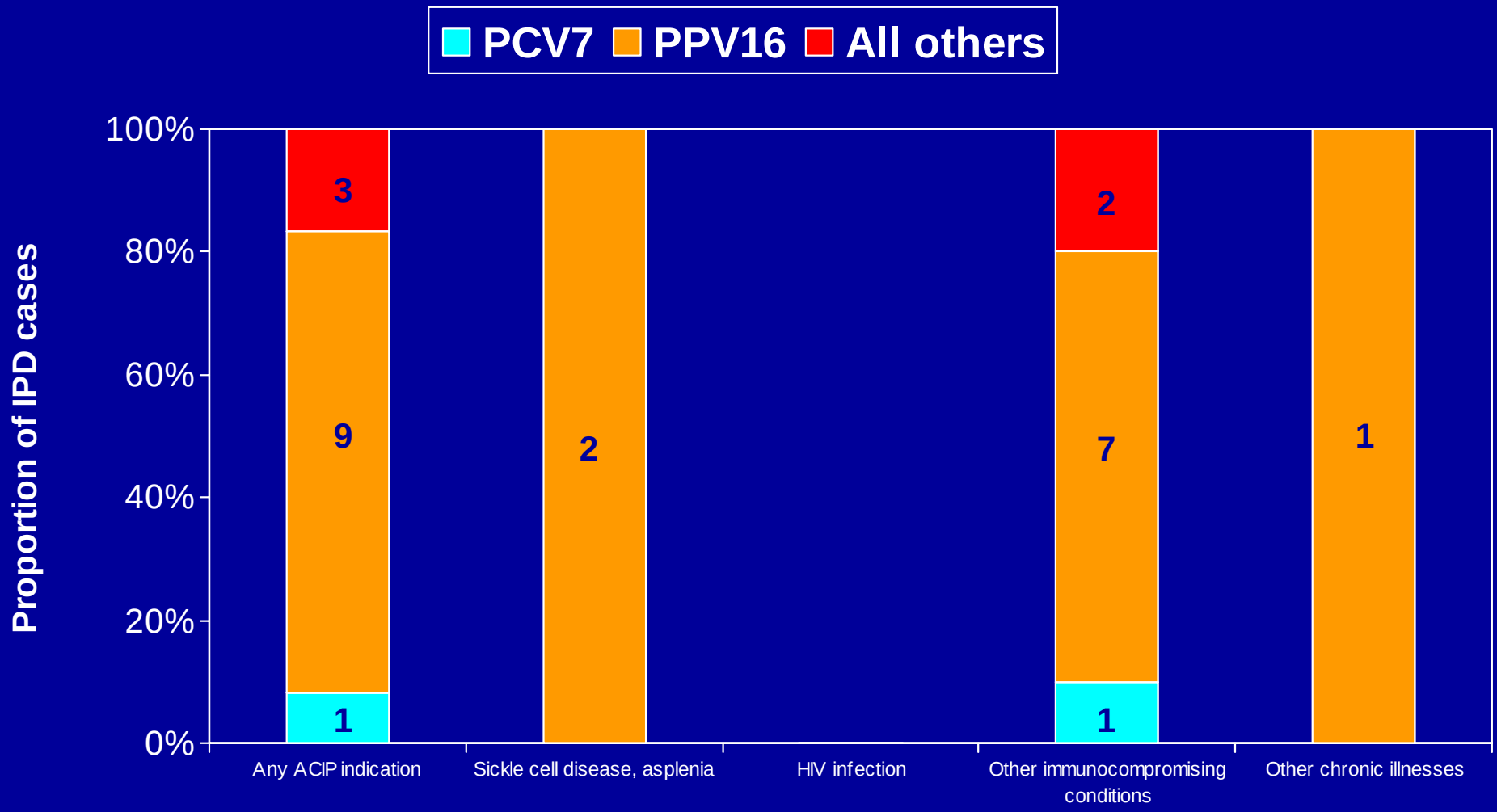
# Rates of invasive pneumococcal disease among children aged 5-9 years, by serotype,1998/99-2006






Data source: CDC, Active Bacterial Core surveillance, unpublished, 2008

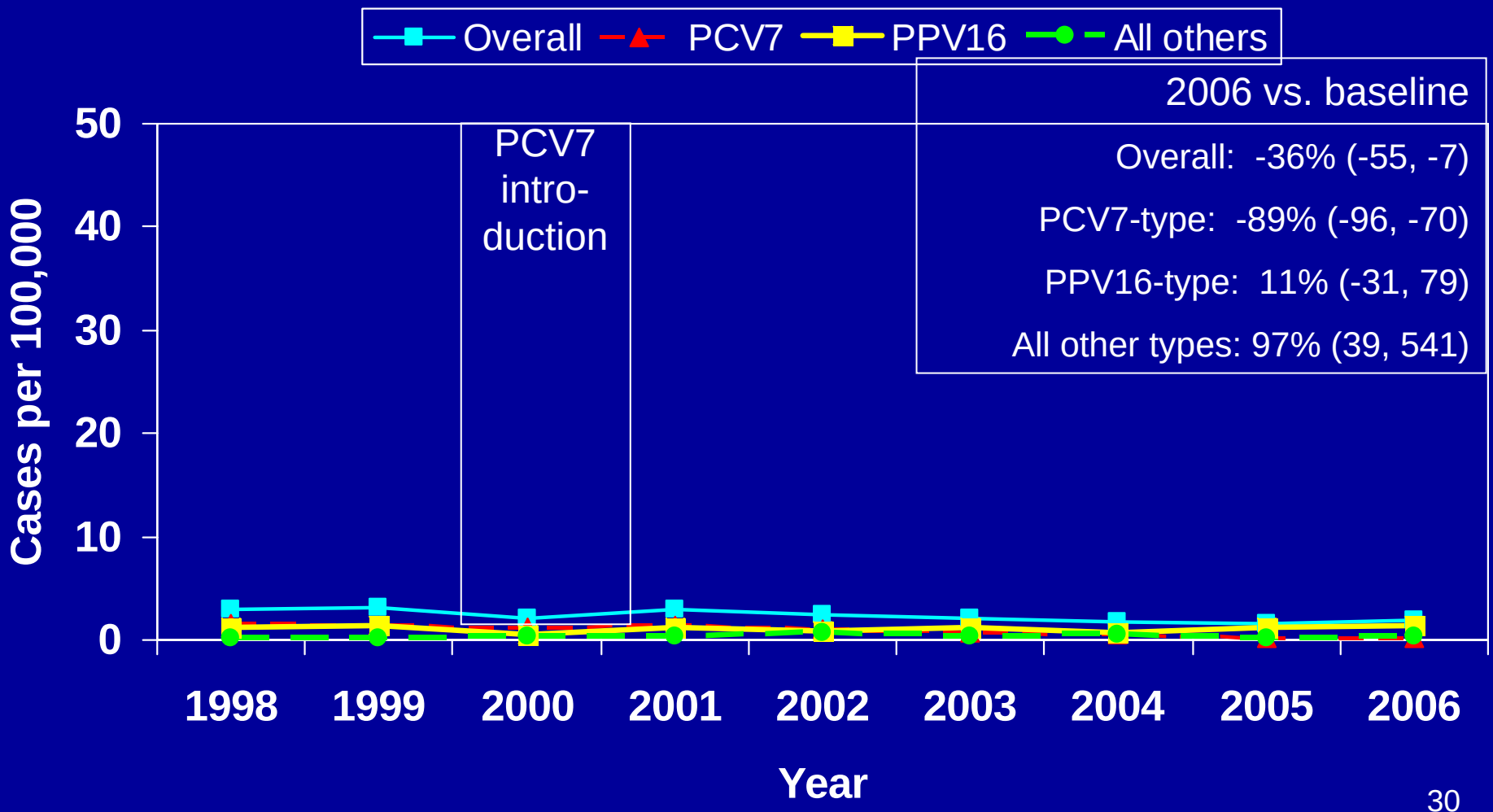
# Proportion of invasive pneumococcal disease cases caused by indicated serotypes among children 5-9 years-old with ACIP indications for PPV23* (N=13), 2006




•Table 2, MMWR 1997;46(No. RR-8):12

•Data source: CDC, Active Bacterial Core surveillance, unpublished, 2008

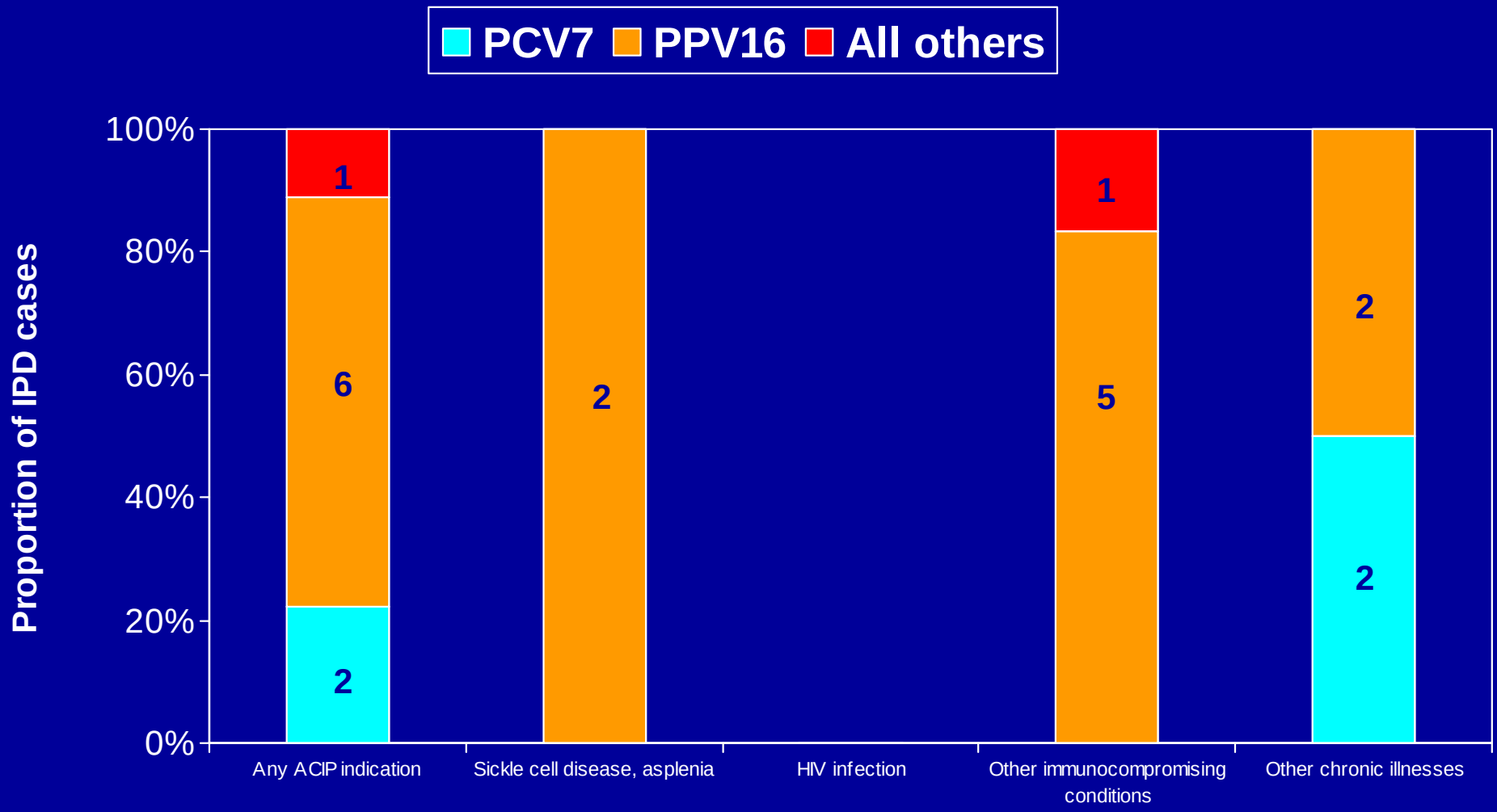
# Rates of invasive pneumococcal disease among children aged 10-19 years, by serotype,1998/99-2006






Data source: CDC, Active Bacterial Core surveillance, unpublished, 2008

# Proportion of invasive pneumococcal disease cases caused by indicated serotypes among children 10-19 years-old with ACIP indications for PPV23* (N=9), 2006




•Table 2, MMWR 1997;46(No. RR-8):12

•Data source: CDC, Active Bacterial Core surveillance, unpublished, 2008

# Evaluation of immunogenicity and safety of combined PCV7/PPV23 schedule in HIV-infected children

- 225 HIV-infected children aged 2-18 years (median 9.6 yr) receiving HAART
  - no PCV7 in infancy;
  - 75% had received PPV23
- Recommended schedule of 2 doses of PCV7 followed by PPV23 (interval 8 weeks)
  - immunogenic: 76-96% and 62-88% had antibody concentrations $\geq$0.5ug/mL and $\geq$1.0 ug/mL) to 5 serotypes
  - No increase in frequency of local or systemic reactions

Abzug et al. Pediatr Infect Dis J 2006;25:920-929

# HIV-infected, school-aged children – Workgroup's considerations

- Among children aged ≥5 years
  - Current rates of PCV7 serotype disease very low
  - Most IPD cases among children with underlying medical conditions are due to PPV23 types
- ACIP has not made a specific recommendation for PCV7 use in children aged ≥5 years for other high risk groups
- PCV7 use in children aged ≥10 years off-label
- Current ACIP and AAP recommendation appropriate:
  - *"Administering PCV7 to older children with high risk conditions is not contraindicated"*
  - *"Current data do not support replacing PPV23 with PCV7 among older children and adults"*

# Proposed recommendation - HIV-infected children

- On the basis of available new immunogenicity and safety data, the Workgroup recommends the following permissive statement:
- *"For HIV-infected children aged 5-17 years on HAART who have NOT been previously immunized with PCV7, practitioners may consider administering 2 doses of PCV7 followed by PPV23"*

# Pneumococcal Vaccines Workgroup Membership 2007-2008

- **ACIP members:**
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  Kathy Neuzil

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  Jennifer Rosen
  Sandy Steiner
  Greg Wallace
  Cynthia Whitney